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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,143	01/22/2002	John Chapman	18242-508 CIP2 (VI-8 CIP2	1572

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EXAMINER	
WINKLER, ULRIKE	

ART UNIT	PAPER NUMBER
1648	

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DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,143	CHAPMAN ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *6-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed December 27, 2005 in response to the Office Action of June 27, 2005 is acknowledged and has been entered. Claims 1-5 and 13-20 are pending and are currently being examined. Claims 6-12 are withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 102

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Meryman et al. (WO 91/04659).

The instant invention is drawn to reducing the amount of an analyte found in mammalian blood the specification defines analyte to include proteins (cytokine, immunoglobulins), small molecules, bacteria, viruses or protozoa. Removal of the extracellular fluid from a red blood cell suspension results in a reduction of an analyte present in the extracellular fluid (a.k.a. serum).

Applicants' arguments have been fully considered but fail to persuade. Applicants' argument is that the reference does not show a starting sample of blood that is greater than 50 ml. In response, Meryman et al. disclose a starting volume of 450 ml of blood drawn from a donor (see example 1, page 26). Thus this argument is not convincing and the rejection is maintained for reasons of record.

An additional argument presented by Applicant is that the amended claim requires that the wash solution contain chloride. In response, ADSOL is a wash solution that comprises chloride (see page 25 lines, 13-18). Also, the reference discloses that the wash solution can be

either ARC8 or a buffered saline solution, with 154 mM NaCl (see example 2, page 27-28). Thus this argument is not convincing and the rejection is maintained for reasons of record.

Meryman et al. discloses the desirability to extend the shelf-life of refrigerated red-cells beyond the current 42 days (see page 5, lines 24-26). The reference discloses the collection of whole blood from a donor that is then centrifuged and resuspended in washing solution, the residual plasma concentration (which carries serum proteins, IgG cytokines and other analytes) is reduced by a factor of 10^2 or 10^3 (see examples 1-5). The preferred embodiment is to pack the red blood cells by centrifugation and separating the red cells from the blood components and resuspending the red cells (see page 25, lines 19-30). The cells that have been stored in solution comprising dextrose, adenenine, manitol, sodium chloride (see table 1) for 42 days can acquire an additional 5 weeks of shelf life by washing the cells and resuspending with a solution containing glucose, sodium citrate, sodium phosphate and adeneine (see table 2 and page 25, lines 13-18). The reference discloses the washing and storage of red cells which includes the removal of blood components and extracellular fluid from the collected whole blood. Because removal of the extracellular fluid from blood removes an analyte found in the serum the instant invention is anticipated by Meryman et al.

Claim Rejections - 35 USC § 103

Claim 1-5 and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maryman et al. (WO 91/04659) and Edson et al. (WO 00/18969).

The instant invention is drawn to reducing the amount of analyte found in a mammalian blood cell suspension using a process of washing the cell suspension which involves

centrifugation and resuspension of the pelleted cell fraction. The blood cells retain viability after storage at 4C for 28 days, or 35 days. Removal of the extracellular fluid results in a reduction of an analyte present in the extracellular fluid (a.k.a. serum). The method of washing reduces the level of extracellular protein (serum albumin, IgG, cytokine) in the blood cells suspension.

Applicants' arguments have been fully considered but fail to persuade. Applicants' argument is that the reference does not show a starting sample of blood that is greater than 50 ml. In response, Meryman et al. disclose a starting volume of 450 ml of blood drawn from a donor (see example 1, page 26). Thus this argument is not convincing and the rejection is maintained for reasons of record.

An additional argument presented by Applicant is that the amended claim requires that the wash solution contain chloride. In response, ADSOL is a wash solution that comprises chloride (see page 25 lines, 13-18). Also, the reference discloses that the wash solution can be either ARC8 or a buffered saline solution, with 154 mM NaCl (see example 2, page 27-28). Thus this argument is not convincing and the rejection is maintained for reasons of record.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F. 2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one of ordinary skill in the art to use the washing and storage procedure as taught by Maryman et al. and apply it to the inactivation

procedure as taught by Edson et al. Each of the references is interested in producing a transfusion blood product that can be used in a patient. By using washing steps that allow for prolonged storage of a blood cell component in conjunction with treating the blood at the same time as taught by Edson et al. would streamline the preparation process of the blood product for use in patients.

Optimizing experimental conditions, including starting volume and repeating the washing steps, falls within the skills of an ordinary artisan. If the timing of adding the modulating compound produces an unexpected result, applicant needs to point out what the unexpected results are. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) and *In re Huang,* 40 USPQ2d 1685 (CAFC 1996) (see paragraph spanning page 1688-1689). The references teach the washing and storage of red cells that includes the removal of blood components and extracellular fluid from the collected whole blood. The use of centrifugation and washing to remove extracellular components from the red blood cell pack is not novel, Applicants contribution over the prior art merely addresses that the washing steps are repeated to achieve a further reduction in the extracellular fluid component. The ordinary artisan would recognize that by adding additional washing steps to the methods disclosed in the prior art the expectation is that this would result in the reduction in the amount of the extracellular fluid found in the original whole blood sample. Applicants have not provided any evidence that their

procedure produces an unexpected result. The instant invention remains rejected as being obvious over Maryman et al. (WO 91/04659) and Edson et al. (WO 00/18969).

Meryman et al. teaches the desirability to extend the shelf-life of refrigerated red-cells beyond the current 42 days (see page 5, lines 24-26). The reference discloses the collection of whole blood from a donor which is then centrifuged and the pellet of packed cells is resuspended in washing solution, the residual plasma concentration (which carries serum proteins, IgG cytokines and other analytes) is reduced by a factor of 10^2 or 10^3 (see examples 1-5). The preferred embodiment is to pack the red blood cells by centrifugation and separating the red cells from the blood components and resuspending the red cells (see page 25, lines 19-30). The cells that have been stored in solution comprising dextrose (a.k.a. glucose), adenine, manitol, sodium chloride (see table 1) for 42 days can acquire an additional 5 weeks of shelf life by washing the cells and resuspending with a solution containing glucose, sodium citrate, sodium phosphate and adenine (see table 2 and page 25, lines 13-18). The reference teaches the washing and storage of red cells, that includes the removal of blood components and extracellular fluid from the collected whole blood. The reference does not teach adding an analyte or therapeutic agent to the whole blood cell mix.

Edson et al. teach separating red blood cell from other blood components such as lymphocytes, neutrophils and platelets as wells as clotting factors and complement. The separation of the red blood cells can be achieved through centrifugation or through automated filtration systems (closed systems) (see page 14, lines 5-22). Blood cells are treated with a small molecule analyte (Pen102) which is an ethyleneimine oligomer inactivating agent. The treated cells are then washed by centrifugation to remove the analyte and removal of the analyte is

monitored using HPLC procedures (see page 24-25). Washing the treated cells reduces the amount of analyte present in the cell suspension (see figure 5) each additional wash results in a further reduction in the analyte. The reference does not teach adding a wash solution that allows for prolonged storage at 4C.

It would have been obvious to one of ordinary skill in the art to use the washing and storage procedure as taught by Maryman et al. and apply it to the inactivation procedure as taught by Edson et al. Each of the references is interested in producing a transfusion blood product that can be used in a patient. By using washing steps that allow for prolonged storage of a blood cell component the treated blood as taught by Edson et al. would have greater applicability in the clinical setting as the process steps can be preformed ahead of time and the product can be analyzed before the treated product is used in a patient. Optimizing experimental conditions, including starting volume and repeating the washing steps, falls within the skills of an ordinary artisan. If the timing of adding the modulating compound produces an unexpected result, applicant needs to point out what the unexpected results are. At this time Applicants have not provided any evidence that their procedure produces an unexpected result. Therefore, the instant invention is obvious over Maryman et al. (WO 91/04659) and Edson et al. (WO 00/18969).

New rejection in view of applicants amendment to the claims:

Claim 1-5 and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maryman et al. (WO 91/04659), Edson et al. (WO 00/18969) and Sharma (U.S. Pat. No. 6,235,239 B1).

The instant invention is drawn to reducing the amount of analyte found in a mammalian blood cell suspension using a process of washing the cell suspension which involves centrifugation and resuspension of the pelleted cell fraction. The blood cells retain viability after storage at 4C for 28 days, or 35 days. Removal of the extracellular fluid (1-5) results in a reduction of an analyte present in the extracellular fluid (a.k.a. serum). The method of washing reduces the level of extracellular protein (serum albumin, IgG, cytokine) in the blood cells suspension.

Meryman et al. teaches the desirability to extend the shelf-life of refrigerated red-cells beyond the current 42 days (see page 5, lines 24-26). The reference discloses the collection of whole blood from a donor which is then centrifuged and the pellet of packed cells is resuspended in washing solution, the residual plasma concentration (which carries serum proteins, IgG cytokines and other analytes) is reduced by a factor of 10^2 or 10^3 (see examples 1-5). The preferred embodiment is to pack the red blood cells by centrifugation and separating the red cells from the blood components and resuspending the red cells (see page 25, lines 19-30). The cells that have been stored in solution comprising dextrose (a.k.a. glucose), adenine, manitol, sodium chloride (see table 1) for 42 days can acquire an additional 5 weeks of shelf life by washing the cells and resuspending with a solution containing glucose, sodium citrate, sodium phosphate and adenine (see table 2 and page 25, lines 13-18). The reference teaches the washing and storage of red cells, that includes the removal of blood components and extracellular fluid from the collected whole blood. The reference does not teach adding an analyte or therapeutic agent to the whole blood cell mix.

Edson et al. teach separating red blood cell from other blood components such as lymphocytes, neutrophils and platelets as wells as clotting factors and complement. The separation of the red blood cells can be achieved through centrifugation or through automated filtration systems (closed systems) (see page 14, lines 5-22). Blood cells are treated with a small molecule analyte (Pen102), which is an ethyleneimine oligomer inactivating agent. The treated cells are then washed by centrifugation to remove the analyte and removal of the analyte is monitored using HPLC procedures (see page 24-25). Washing the treated cells reduces the amount of analyte present in the cell suspension (see figure 5) each additional wash results in a further reduction in the analyte. The reference does not teach adding a wash solution that allows for prolonged storage at 4C.

Sharma teaches a method of disinfecting blood by introducing a disinfectant into a blood sample, mixing the composition with the blood, separating the cellular component from the supernatant and subjecting the cellular component to an extraction to effectively remove the disinfectant composition component. The separation can be achieved by filtration, centrifugation and decantation. The extraction technique can be achieved using an immunological procedure washing or chromatographic technique. (see claims 8-19). Treated cells can also be washed with a sterile phosphate buffered saline solution and the packed red cells can be reconstituted to 50 ml volume in ADSOL. The samples are then stored for 20 days in the refrigerator and then tested for deformity (see example 18). The viability of the cells was tested after a 20 day storage in the refrigerator. The reference teaches using a composition for the purpose of disinfecting blood or a component sample of blood for the purpose of using the component in transfusions (see column 2, lines 50-55, and example 4). The reference teaches using a washing procedure and a storage

procedure that would result in a red blood cell suspension that can be stored for up to 42 days (see Maryman et al. above). The reference does not teach adding an ethyeleneimine derivative as a disinfecting agent.

It would have been obvious to one of ordinary skill in the art to use the washing and storage procedure as taught by Maryman et al. and apply it to the inactivation procedure as taught by Edson et al or Sharma. In addition Sharma teaches using a washing procedure and a storage procedure that would result in a red blood cell suspension that can be stored for up to 42 days (see Maryman et al. above). Each of the references is interested in producing a transfusion blood product that can be used in a patient. By using washing steps that allow for prolonged storage of a blood cell component the treated blood as taught by Edson et al. would have greater applicability in the clinical setting as the process steps can be preformed ahead of time and the product can be analyzed before the treated product is used on a patient. Optimizing experimental conditions, including starting volume and repeating the washing steps, falls within the skills of an ordinary artisan. If the timing of adding the modulating compound produces an unexpected result, applicant needs to point out what the unexpected results are. Therefore, the instant invention is obvious over Maryman et al. (WO 91/04659), Edson et al. (WO 00/18969) and Sharma (U.S. Pat. No. 6,235,239 B1).

Conclusion

No claims allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The cited art below teaches the use of ADSOL solution and long term storage of red

blood cells. The reference teach that red cells stored in ADSOL are viable past 21 of storage in the refrigerator :

Leonart et al. Enzymes and membrane protein of ADSOL-preserved red blood cells. Sao Paulo Medical Journal (2000) Vol. 118, No. 2, pages 41-45.

Simon et al. Effects of AS-3 nutrient-additive solution on 42 and 49 days of storage of red cells. Transfusion (1987) Vol. 27, pages 178-182.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov]. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PH.D.
PRIMARY EXAMINER